

Attorney's Docket No. 029395-002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)

Jean-Luc IMLER et al.)

Application No.: 08/379,452)

Filed: January 26, 1995 (corrected))

For: DEFECTIVE ADENOVIRUSES)
AND CORRESPONDING)
COMPLEMENTATION LINES)

Group Art Unit: 1632

Examiner: S. Priebe

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GROUP 1700

DECLARATION UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Majid Mehtali, do hereby declare:

THAT, I am employed by Transgene S.A., the Assignee of the above-identified application, as the Head of the Gene Therapy Department;

THAT, I have received an Engineer Diploma in Biotechnology in 1985 from the European School of Biotechnology of the Upper Rhine Region, Strasbourg, France. In 1988, I received a Ph.D. in Molecular Biology at the Institute of Molecular Genetics at the University of Strasbourg, France;

THAT, a copy of my Curriculum Vitae is attached hereto;

THAT, I am a joint inventor of the subject matter disclosed and claimed in the above-referenced application and I have reviewed and am familiar with the contents of U.S. Patent Application Serial No. 08/379,452;

THAT, I have reviewed and am familiar with the Examiner's rejection of the claims alleging that the nucleotide sequence of GenBank accession number M73260 must be included in the application in order for applicants to recite the nucleotide residue numbers in the claims;

THAT, the claims in the present application which refer to nucleotide residue numbers refer to the human adenovirus type 5 sequence described in the specification as being disclosed in GenBank under accession number M73260. See, for example, pages 4, 10, 19 and 24 of the originally filed specification.

THAT, reference to the GenBank accession number reasonably conveys to one of ordinary skill in the art that the inventors were in possession of the nucleotide sequence for human adenovirus type 5 at the time the earliest French priority application was filed.

THAT, the nucleotide sequence having GenBank accession number M73260 was originally deposited by Dr. Chroboczek's research group and described in the following journal article: Chroboczek et al., *Virology*, 186(1):280-285 (1992).

THAT, I contacted Dr. Chroboczek and obtained a copy of the human adenovirus type 5 nucleotide sequence which was deposited with GenBank and assigned accession number M73260.

THAT, when I contacted Dr. Chroboczek, she indicated that she was not aware of any changes to the nucleotide sequence since it was originally deposited in GenBank.

THAT, the nucleotide sequence obtained from Dr. Chroboczek was compared with the nucleotide sequence currently provided by GenBank on-line via the Internet.

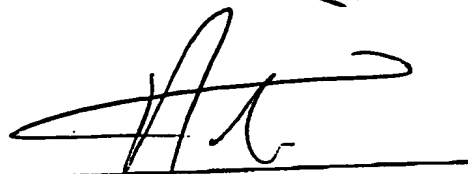
THAT, as a result of this comparison, I have determined that there have been no changes to the human adenovirus type 5 nucleotide sequence since it was originally filed in GenBank.

THAT, a representative from TRANSGENE, S.A., the assignee of the present application, contacted GenBank to verify that no changes have been made to the human adenovirus type 5 nucleotide sequence having accession number M73260 since it was originally deposited by Dr. Chroboczek's research group.

THAT, GenBank indicated that the record for accession number M73260 had been updated in 1996, however, this update reflected the changes which were made by the International Committee on Taxonomy of Viruses not any changes to the nucleotide sequence.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application or any patent issuing thereon.

May 31st, 1999
Date


Majid Mehtali

CURRICULUM VITAE

Majid MEHTALI, PhD

PERSONNAL

Marital Status : Married, One child
Nationality : French
date of birth : March 14th, 1962

BUSINESS ADDRESS

TRANSGENE S.A.
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PRIVATE ADDRESS

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67400 Illkirch, France
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E-mail: mehtali@hotmail.com

EDUCATION :

High School, Saint-Louis, France

1980 : Baccalaureat D (Mathematics, Physics, Biology)

European School of Biotechnology of the Upper rhine Region, Strasbourg, France
1982-1985 : Engineer Diploma in Biotechnology

University of Strasbourg, France

1980-1982: Diploma of General Biological University Studies (DEUG. B)
1983: Licence in Biochemistry
1984: Maitrise in Biochemistry
1985: D.E.A. in Molecular Biology (equivalent to Msc)
1985-1988: PhD in Molecular Biology at the Institute of Molecular Genetics (Director: Pr. P. Chambon). Topic: *in vitro* and *in vivo* (in transgenic mice) analysis of the role of specific regulatory sequences from housekeeping genes

PROFESSIONAL EXPERIENCE :

1984: 3 months period at Roche (Basel) in the laboratory of Dr. R. Then (Pharmaceutical Research Dpt); topic: biochemical analysis of the bacterial porins isolated from antibiotic-resistant strains.
1985: 9 months period at Rhône-Mérieux Company (Lyon, France) in the laboratory of

Dr. G. Chappuis; topic: identification and biochemical characterization of the pathogenic agents (later shown to belong to the Pestiviruses virus family) responsible for bovine and porcine diseases.

1988:

Staff Scientist at Transgene S.A.

Research projects:

- (i) development of novel transgenic animal models (mice and rabbits) for the evaluation of potential anti-HIV1 treatments and characterisation of the role of major HIV regulatory proteins in AIDS pathogenesis;
- (ii) production and evaluation in rhesus and cynomolgus macaques of various recombinant AIDS vaccine candidates (Live attenuated viruses, recombinant purified viral proteins, poxvirus-derived vaccines, pseudovirions,...).

1991-1992:

Head of the Virology-Immunology department at Transgene S.A.

Research projects:

- (i) development and evaluation of candidate AIDS vaccines;
- (ii) development and evaluation of new immunotherapeutic approaches for breast cancer.

1992-1998:

Head of the Gene Therapy department at Transgene S.A.

Research projects:

- (i) development of novel generations of safer and more efficient viral (human and animal adenovirus, murine retrovirus, simian lentivirus) and cellular vectors for gene therapy;
- (ii) development and evaluation *in vitro* and *in vivo* of gene therapy strategies for cancer, AIDS, Hemophilia and cardiovascular diseases;

PUBLICATIONS :

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A ubiquitous expression vector, pHMG, based on a housekeeping gene promoter.
Nucl. Acids Res. 17 (1989), 8389.
- 2) **Tomasetto, C. Wolf, C., Rio, M.C., Mehtali, M., LeMeur, M., Gerlinger, P., Chambon, P. & Lathe, R.**
Breast cancer protein PS2 synthesis in mammary gland of transgenic mice and secretion into milk.
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- 3) **Mehtali, M. LeMeur, M. & Lathe, R.**
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Gene 91 (1990), 179-184.
- 4) **Pons, M., Gagne, D., Nicolas, J.C. & Mehtali, M.**
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BioTechniques 9 (1990), 450-459.
- 5) **Kieny, M.P., Aubertin, A.M. & Mehtali, M.**
Approaches to vaccination against primate immunodeficiency viruses infection. In "Retroviruses of Human AIDS and Related Animal Diseases", Ed. Girard, M. & Valette, L., Fondation Marcel Merieux: Lyon, France (1990). 171-175.
- 6) **Bchini, O., Andres, A.C., Schubaur, B., Mehtali, M. LeMeur, M., Lathe, R. & Gerlinger, P.**
Precocious mammary gland synthesis in transgenic mice ubiquitously expressing human growth hormone.
Endocrinology 128 (1991), 539-546.
- 7) **Bchini, O., Mehtali, M. & Lathe, R.**
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J. Molecular Endocrinology 6 (1991), 129-135.
- 8) **Pancré, V., Pierce, R.J., Fournier, F., Mehtali, M., Delanoye, A., Capron, A. & Auriault, C.**
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- 9) **Mehtali, M., Munschy, Caillaud, J.M., & Kieny, M.P.**
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In "Retroviruses of Human AIDS and Related Animal Diseases", Ed. Girard, M. & Valette, L., Fondation Marcel Merieux: Lyon, France (1991). 25-30.

- 10) Mehtali, M., Acres, B., & Kieny, M.P.
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- 11) Pons, M., Gagne, D., Nicolas, J.C. & Mehtali, M.
Characterization of a new bioluminescent cellular model of response to estrogens. In "Bioluminescence and Chemoluminescence: current Status", Eds Stanley, P.E. and Kriska, L.J., John Wiley & Sons, Chichester, New-York, Brisbane, Toronto, Singapore (1991). 51-54.
- 12) Mehtali, M. Munschy, Ali-Hadji, D., & Kieny, M.P.
A novel transgenic mouse model for the *in vivo* evaluation of anti-HIV1 drugs. AIDS Res. & Hum. Retroviruses 8 (1992), 1959-1965.
- 13) Mehtali, M., Benavente, A., Beyer, C., Gloeckler, L., Schmitt, D., Fischer, F., Dott, K., Sene, C., Kolbe, H., Hurtrel, B., Girard, M., Venet, A., Rivière, Y., Aubertin, A.M. & Kieny, M.P.
Different approaches towards an HIV vaccine using SIV as a model. In "Retroviruses of Human AIDS and Related Animal Diseases", Ed. Girard, M. & Valette, L., Fondation Marcel Merieux: Lyon, France (1992). 247-250.
- 14) Kieny, M.P., Aubertin, A.M., Benavente, A., Schmitt, D., Dott, K., Beyer, C., Kirn, A., Fischer, F., Hurtrel, B., Rivière, Y., Venet, A. & Mehtali, M.
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- 15) Liska, V., Spehner, D., Mehtali, M., Schmitt, D., Kirn, A. & Aubertin, A.M.
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- 16) M. Mehtali.
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- 18) Estaquier, J., Idziorek, T., De Bels, F., Barré-Sinoussi, F., Hurtrel, B., Aubertin, A.M., Venet, A., Mehtali, M., Muchmore, E., Michel, P., Mouton, Y., Girard, M. & Ameisen, J.C.
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J. Gen. Virology (1995), 76, 1327-1336.
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Gene (1995), 159, 279-280.
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Cancérologie aujourd'hui (1995) 4, 242-252.
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Annales d'Endocrinologie (1995) 56, 571-574.
- 25) Pavirani, A., Schatz, C. and Mehtali, M.
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In : Transgenic animals - generation and use (eds L.-M. Houdebine). Haarwood Academic Publishers GmbH, Chur - CH (1997), 427-433.
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- 39) Michou, A.I., Santoro, L., Christ, M., Julliard, V., Pavirani, A. and Mehtali, M.
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In : The Biotherapy of Cancer: from immunotherapy to gene therapy - (eds S. Chouaib).
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Experimental gene therapy : the transfer of Tat-inducible interferon genes protects human cells against HIV-1 challenge *in vitro* and *in vivo* in severe combined immunodeficient mice.
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- 42) Christ, M., Lusky, M., Stoeckel, F., Dreyer, D., Dieterle, A., Michou, A.I., Pavirani, A. and Mehtali, M.
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- 43) Michou, A.I., Christ, M., Pavirani, A. and Mehtali, M.
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Gene therapy for AIDS : *In vitro* and *in vivo* inhibition of viral replication by transfer of HIV-1-inducible interferon genes.
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- 45) Dunn, C.S., Hurtrel, B., Beyer, C., Gloeckler, L., Ledger, T.N., Moog, C., Kieny, M.P., Mehtali, M., Schmitt, D., Gut, J.P., Kirn, A. and Aubertin, A.M.
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- 47) Lusky M., Christ M., Rittner K., Dieterle A., Dreyer D., Mourrot B., Schultz H., Stoeckel F., Pavirani A., and Mehtali M.

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- 52) Santis G., Legrand V., Hong S.S., Davison E., Kirby I., Imler J.L., Finberg R.W., Bergelson J.M., Mehtali M. and Boulanger P.
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Submitted.
- 53) Roschlitz C., Jantscheff P., Bongartz G., Dietrich P.Y., Schatz C., Mehtali M., Courtney M., Tartour E., Dorvarl T., Fridman W.H. and Herrmann R.
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Gene Ther. (1998), In Press
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Submitted.
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Hum. Gene Ther. (1998), In Press
- 56) Leroy P., Slos P., Homann H., Erbs P., Poitevin Y., Regulier E., Quintin-Colonna

F., Devauchelle P., Roth C., Pavirani A. and Mehtali M.
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- 57) Regulier E. and Mehtali M.
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J. Virol. (1998), In Press